

## Environmental Health and Safety (EH&S) of Silica Nanomaterials

In recent years, studies revealing the toxicity of carbon-based nanomaterials have led to concerns over the potential toxic effects of other nanomaterials. In order to address these concerns, a concise review of toxicity studies performed on carbon materials is given followed by a comparison of similar studies on silica materials.

Multi-walled carbon nanotubes (MWCNTs) and carbon nanofibers have been found to be significantly toxic to human lung tumor cells as early as 24 h after exposure [1]. Single-walled nanotubes (SWCNTs) have also been found to be toxic in some systems [e.g., 2,3], although a recent report examining SWCNTs in mice revealed no apparent toxicity over a four-month period [4]. Due to these and other conflicting reports on the toxicity of CNTs [4,5], studies involving the application of CNTs for biomedical applications are still being conducted [e.g., 6,7]. In order to further the use of CNTs for such applications, researchers have functionalized the surface of CNTs, rendering them benign [5]. Unfortunately, concerns that functionalized CNTs may revert back to a toxic state if the functional group detaches has limited the pursuit of the biomedical applications of these modified CNTs.

The toxicity of other forms of nanocarbon has also been reported [e.g., 1,8,9]. In one study juvenile largemouth bass were exposed to C60 fullerenes (aka buckyballs) [9]. Within 48 h of exposure to a 0.5 parts per million (ppm) aqueous suspended colloid, bass were found with significant lipid peroxidation in the brains, as well as marginal depletion of glutathione in the gills. Another study of human lung tumor cells showed that carbon nanoparticles are even more toxic than MWCNTs and carbon nanofibers [1]. In yet another study, it was observed that carbon nanoparticles accumulate adjacent to the nuclear membrane and within the nucleus when internalized into human monocyte macrophages and possibly lead to DNA damage [8].

Given the mounting evidence demonstrating the toxicity of carbon nanoparticles, efforts to develop carbon nanoparticles for biomedical applications have dropped off significantly in recent years.

Silica (glass) nanoparticles are an extremely popular type of nanomaterial for biomedical applications due to their well known non-toxic biocompatibility [e.g., 10-13]. A recent study by Adili *et al.* [10] showed that HEP-2 and HeLa cells remain viable when exposed to a silica nanoparticle concentration of 190 µg/ml. This non-toxic result for such a high concentration of silica nanoparticles is in stark contrast to the high toxicity observed from a ppm suspension of C60 fullerenes. Chen and von Mikecz [14] also observed that cell viability was not compromised by exposure to silica nanoparticles, although a significant reduction in the synthesis of RNA and the replication of DNA was noted. So while silica nanoparticles are non-toxic at fairly high concentrations, they can interfere with cell functions. In spite of reduction in synthesis and replication of RNA and DNA, the relative non-toxicity and biocompatibility of silica nanoparticles makes them an excellent candidate for biomedical applications.

A recent study comparing the toxicity of nanowires and nanoparticles made from silica on human tissue culture cells demonstrated that at concentrations below 190 µg/mL neither nanowires nor nanoparticles induced a toxic effect when added to cells [10]. Surprisingly, nanowires but not nanoparticles exhibited significant toxicity at concentrations greater than 190 µg/mL [10]. These results indicate that the silica nanowires are more toxic than silica nanoparticles at equivalent quantities, however the reason for this differential toxicity is not well understood, i.e., whether toxicity is a function of morphology, surface chemistry, or the amount of material internalized. Considering that the quantity of material exposed to the cells in this study was enough to fill 10% of the volume of each cell with silica material, it would be surprising if toxic effect were not observed if complete internalization of the material occurred. Therefore it is most likely that the

differential toxicity observed was due to more efficient internalization of the nanowires than the nanoparticles, resulting in greater stress on the cells and therefore necrotic cell response. Unfortunately, this study did not include a determination of the amount of material actually internalized by the cells. The fact that toxic effects were only observed after the introduction of such large quantities of material is a testament to the non-toxic biocompatibility of silica nanowires and silica nanomaterials in general. This assertion is consistent with other toxicity results in which exposure of lower quantities of nanowires to cells were indistinguishable from cell culture controls [15].

While toxicity studies have not been performed on the silica Nanospring material, it should be noted that each Nanospring is comprised of multiple silica nanowires and therefore Nanosprings might be expected to be comparable to silica nanowires in biocompatibility. However, differential toxicity observed between silica nanowires and nanoparticles suggests that minor differences in toxicity might be observed between silica nanowires and Nanosprings. Collectively, the studies done thus far seem to indicate that silica is a non-toxic, biocompatible material regardless of size and morphology especially when compared to carbon-based nanomaterials.

GoNano Technologies Inc. is committed to both human and environmental safety. Our goal is the production of application specific materials that pose no health risk to humans when used for their intended purpose. Our nanomaterials are produced in such a way as to reduce or eliminate the potential for materials to become airborne. This is accomplished using techniques that result in materials that are firmly attached to a substrate and therefore are not easily detached even when exposed to high speed fluid flows through the mat [16]. GoNano Technologies, Inc. continues to monitor regulations from the EPA and other agencies to ensure strict compliance with the most current federal regulations.

#### References Cited

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